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Antinociceptive and Immune Effects of Delta-9-tetrahydrocannabinol or Cannabidiol in Male Versus Female Rats with Persistent Inflammatory Pain.

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Supplemental Figure Legends

Supplemental Figure 1 Effects of THC (A) and CBD (B) on the von Frey test on Day 8, with data pooled across sexes. The mechanical threshold was ~ 50% BL in vehicle-treated rats for both the THC experiment (A) and the CBD experiment (B). Rats previously treated with THC showed greater allodynia compared with rats that previously received vehicle. Previous treatment with CBD did not alter allodynia on Day 8. Each bar is the mean \pm 1 S.E.M. of 16-24 rats. *significantly different from vehicle-treated controls ($p < 0.05$).

Supplemental Figure 2 Effects of THC (A) and CBD (B) on the Hargreaves test on Day 8, with data pooled across sexes. Previous treatment with THC or CBD did not alter thermal antinociception on Day 8. Each bar is the mean \pm 1 S.E.M. of 16-24 rats.

Supplemental Figure 3 Effects of THC (A) and CBD (B) on the incapacitance (weight-bearing) test on Day 8, with data pooled across sexes. Previous treatment with THC (A) but not CBD (B) increased weight-bearing on the inflamed paw on Day 8. Each bar is the mean \pm 1 S.E.M. of 16-24 rats. *significantly different from vehicle-treated controls ($p < 0.05$).

Supplemental Figure 4 Effects of THC (A & B) and CBD (C & D) on paw thickness (edema) in male (A & C) and female (B & D) rats on Day 8. Previous treatment with THC (A & B) did not alter paw thickness on Day 8. Previous treatment with CBD 10 mg/kg decreased paw thickness in females (D) but not males (C). Each bar is the mean

± 1 S.E.M. of 8-12 male or female rats. *significantly different from same-sex, vehicle-treated controls ($p < 0.05$).

Supplemental Figure 5 CBD effects on the paw thickness (edema) test on Day 4 (240-min timepoint), with data pooled across sexes. CBD 10 mg/kg decreased paw thickness and this effect did not differ between acutely vs. repeatedly treated rats. Each bar is the mean ± 1 S.E.M. of 16-24 rats. *significantly different from vehicle-treated controls ($p < 0.05$).

Supplemental Figure 6 THC effects on the locomotor activity test on Day 4 (means of Day 4 time course data) pooled across sexes. Both acute and repeated THC decreased locomotor activity. Each bar is the mean ± 1 S.E.M. of 16-24 rats. *significantly different from vehicle-treated controls ($p < 0.05$).

Supplemental Figure 7 Effects of THC (A) and CBD (B) on the locomotor activity test on Day 8, with data pooled across sexes. Rats previously treated with THC had decreased locomotor activity compared with rats that previously received vehicle, and this effect did not differ in rats that received THC once on Day 4 compared with rats that received THC repeatedly on Days 1-4. Previous treatment with CBD did not alter locomotor activity on Day 8. Each bar is the mean ± 1 S.E.M. of 16-24 rats.

*significantly different from vehicle-treated controls ($p < 0.05$).

Supplemental Figure 8 Spleen weights from male (A) and female (B) rats on Day 4 (Experiment 2). CFA increased spleen weight in males, but not females. Neither THC nor CBD altered spleen weight in either sex, regardless of pain state. Each bar is the mean \pm 1 S.E.M. of 7-8 male or female rats. *significantly different from same sex, mineral oil + vehicle-treated group ($p < 0.05$).

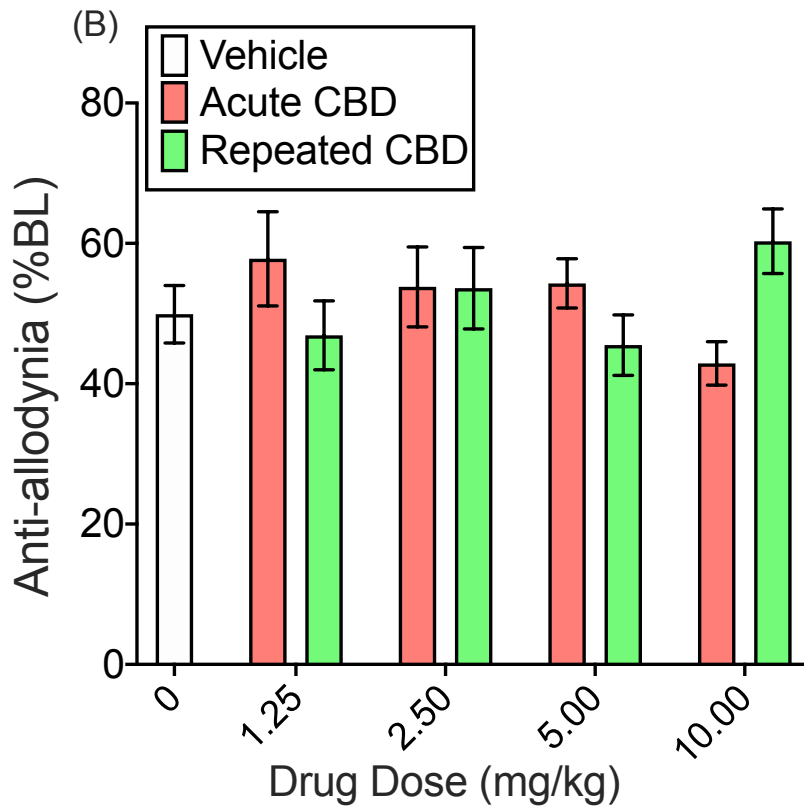
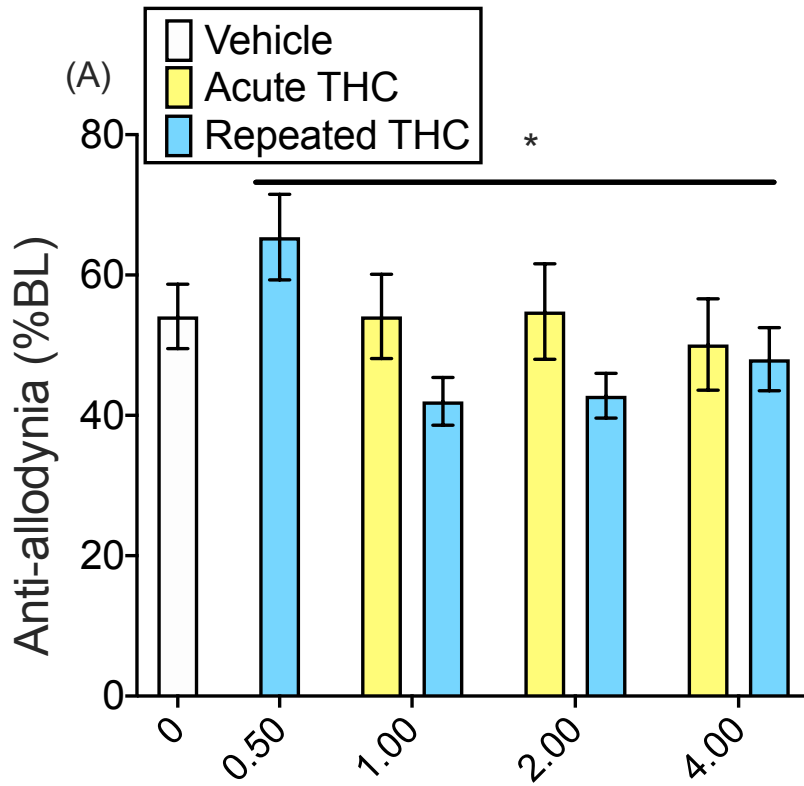
Supplemental Table 1

<i>Table of planned comparisons for the behavioral experiment with THC on Day 4. *Significant effect</i>				
Data	Comparison	df	F	p
Von Frey % BL means	Sex x THC dose x Chronicity	3	0.26	0.854
	Sex x THC dose	4	0.77	0.550
	Sex x Chronicity	1	0.10	0.751
	THC dose x Chronicity	3	1.89	0.134
	Chronicity	1	0.41	0.522
	Sex	1	5.16	0.025*
	THC dose	4	19.49	0.000*
Hargreaves %BL means	Sex x THC dose x Chronicity	3	2.69	0.049*
	Sex x THC dose	4	2.84	0.026*
	Sex x Chronicity	1	4.01	0.047*
	THC dose x Chronicity	3	5.17	0.002*
	Chronicity	1	16.71	0.000*
	Sex	1	2.77	0.098
	THC dose	4	22.96	0.000*
Weight-bearing %BL means	Sex x THC dose x Chronicity	3	0.51	0.675
	Sex x THC dose	4	0.60	0.661
	Sex x Chronicity	1	1.56	0.214
	THC dose x Chronicity	3	1.72	0.165
	Chronicity	1	4.66	0.032*
	Sex	1	4.17	0.043*
	THC dose	4	4.66	0.031*
Locomotor activity % BL means	Sex x THC dose x Chronicity	3	0.43	0.733
	Sex x THC dose	4	0.60	0.664
	Sex x Chronicity	1	0.20	0.658
	THC dose x Chronicity	3	1.33	0.269
	Chronicity	1	0.92	0.340
	Sex	1	1.26	0.264
	THC dose	4	14.38	0.000*
Paw thickness %BL (measured only at 240 min post-injection)	Sex x THC dose x Chronicity	3	0.68	0.569
	Sex x THC dose	4	0.51	0.767
	Sex x Chronicity	1	1.83	0.178
	THC dose x Chronicity	3	0.49	0.691
	Chronicity	1	3.47	0.235
	Sex	1	4.85	0.029*
	THC dose	4	1.41	0.235

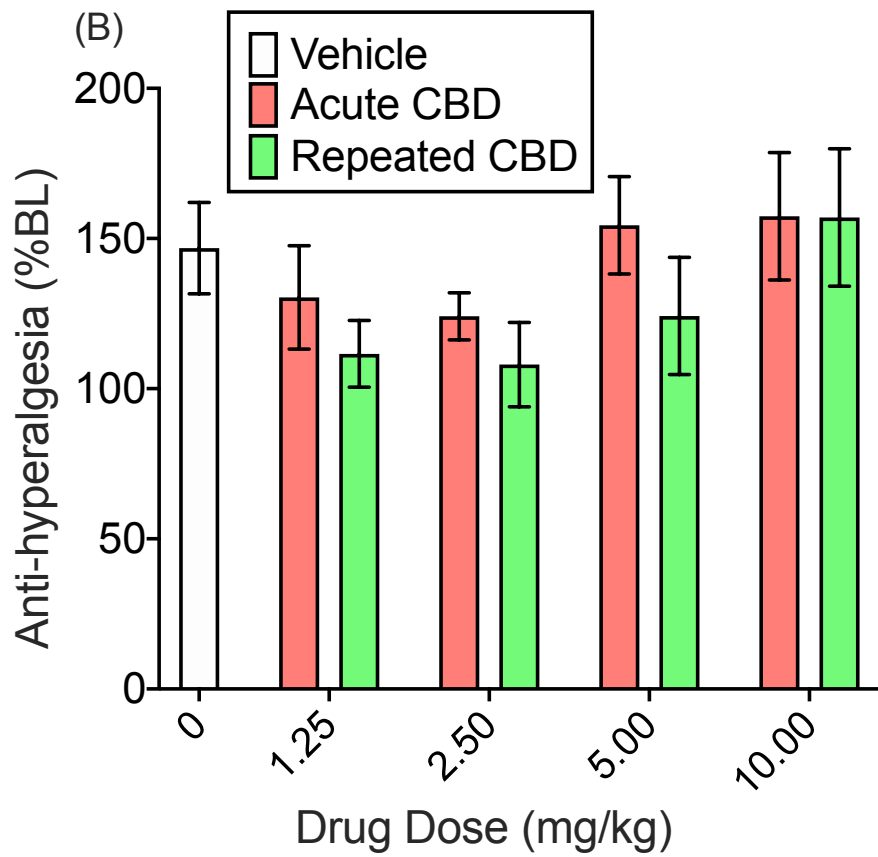
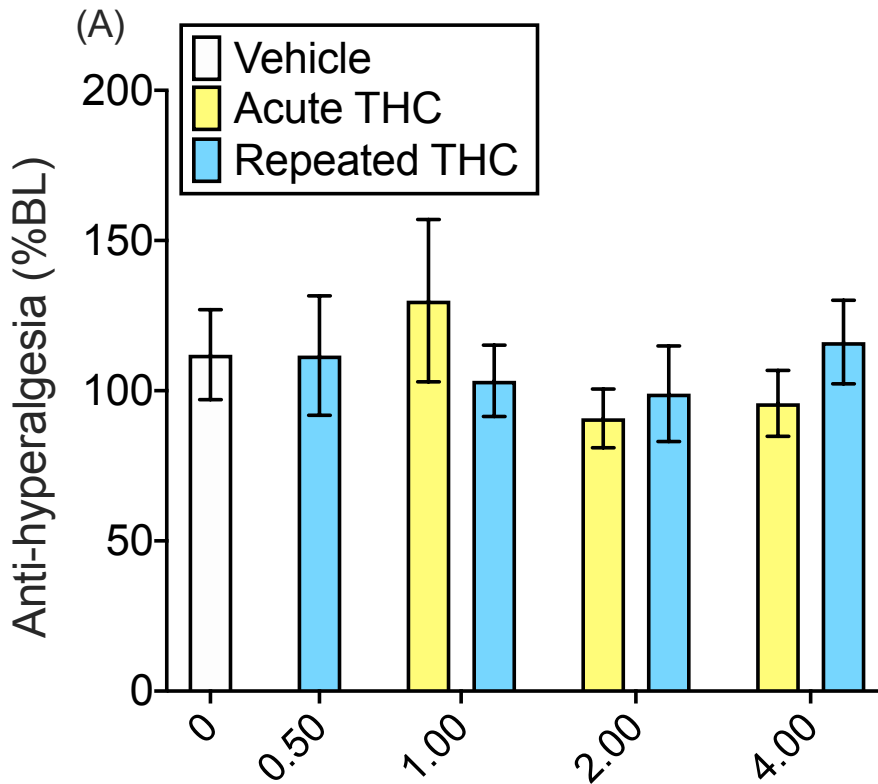
Supplemental Table 2

<i>Table of planned comparisons for the behavioral experiment with CBD on Day 4. *Significant effect</i>				
Data	Comparison	df	F	p
Von Frey % BL means	Sex x CBD dose x Chronicity	4	1.40	0.235
	Sex x CBD dose	4	1.07	0.374
	Sex x Chronicity	1	0.06	0.801
	CBD dose x Chronicity	4	0.85	0.498
	Chronicity	1	0.00	0.995
	Sex	1	0.20	0.656
	CBD dose	4	2.51	0.043*
Hargreaves %BL means	Sex x CBD dose x Chronicity	4	1.23	0.298
	Sex x CBD dose	4	0.78	0.540
	Sex x Chronicity	1	0.47	0.494
	CBD dose x Chronicity	4	0.19	0.944
	Chronicity	1	1.15	0.285
	Sex	1	3.07	0.081
	CBD dose	4	0.38	0.824
Weight-bearing %BL means	Sex x CBD dose x Chronicity	4	1.45	0.221
	Sex x CBD dose	4	0.68	0.609
	Sex x Chronicity	1	0.08	0.774
	CBD dose x Chronicity	4	1.99	0.097
	Chronicity	1	0.15	0.701
	Sex	1	0.51	0.478
	CBD dose	4	2.49	0.045*
Locomotor activity % BL means	Sex x CBD dose x Chronicity	4	0.37	0.827
	Sex x CBD dose	4	1.31	0.269
	Sex x Chronicity	1	0.63	0.427
	CBD dose x Chronicity	4	0.20	0.938
	Chronicity	1	0.91	0.342
	Sex	1	0.33	0.567
	CBD dose	4	2.64	0.035*
Paw thickness %BL (measured only at 240 min post-injection)	Sex x CBD dose x Chronicity	4	0.50	0.737
	Sex x CBD dose	4	1.44	0.223
	Sex x Chronicity	1	1.85	0.175
	CBD dose x Chronicity	4	0.72	0.582
	Chronicity	1	2.67	0.104
	Sex	1	7.28	0.008*
	CBD dose	4	2.72	0.031*

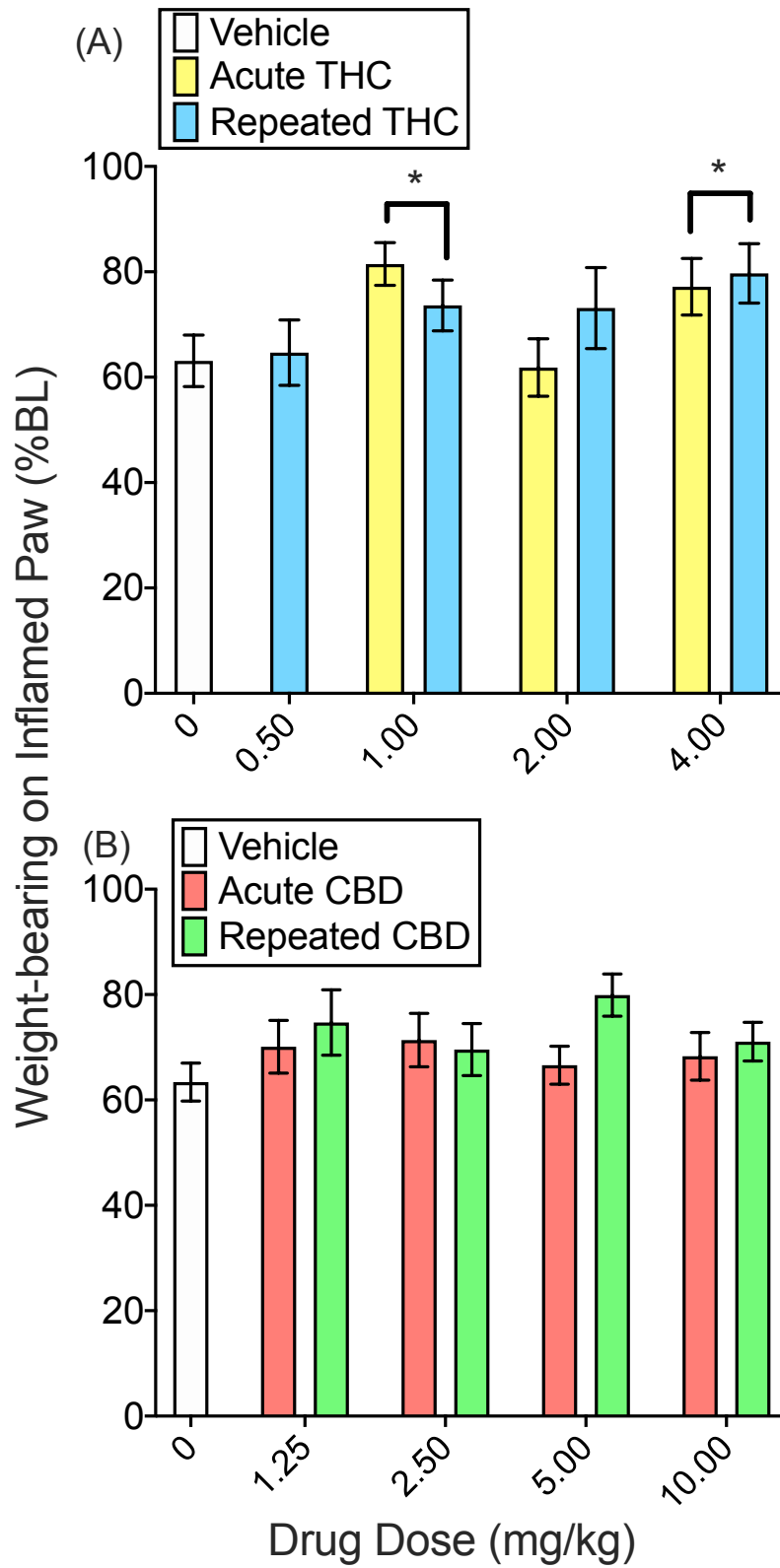
Supplemental Figure 1



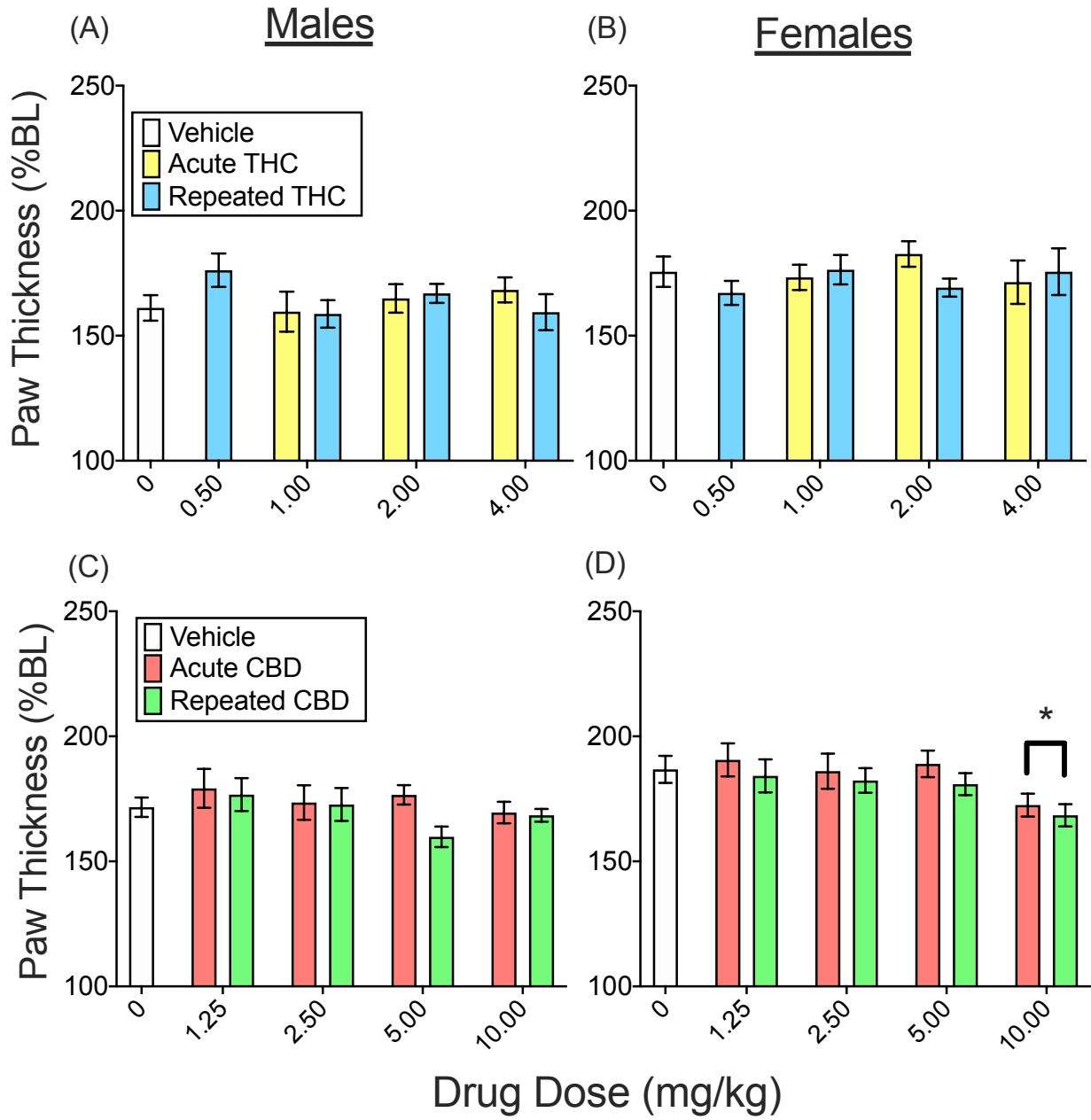
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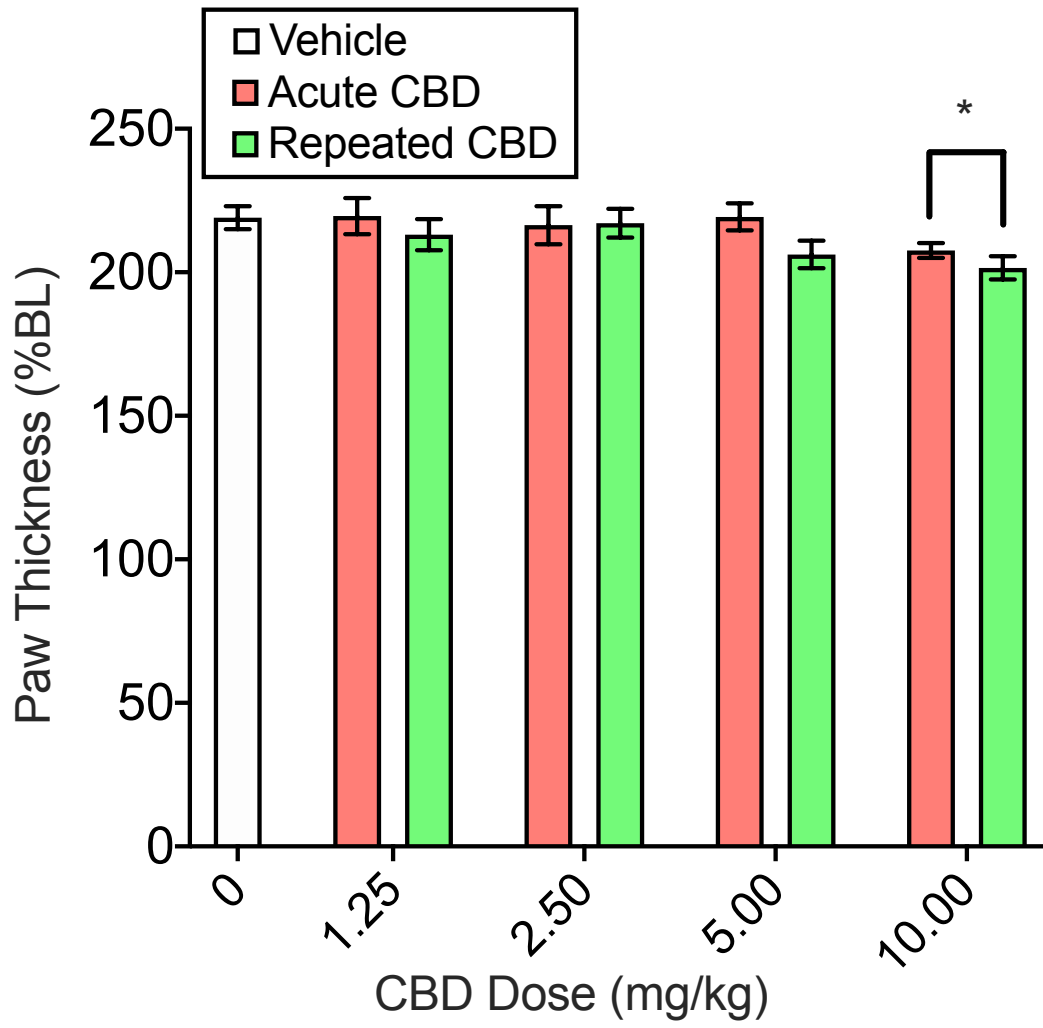
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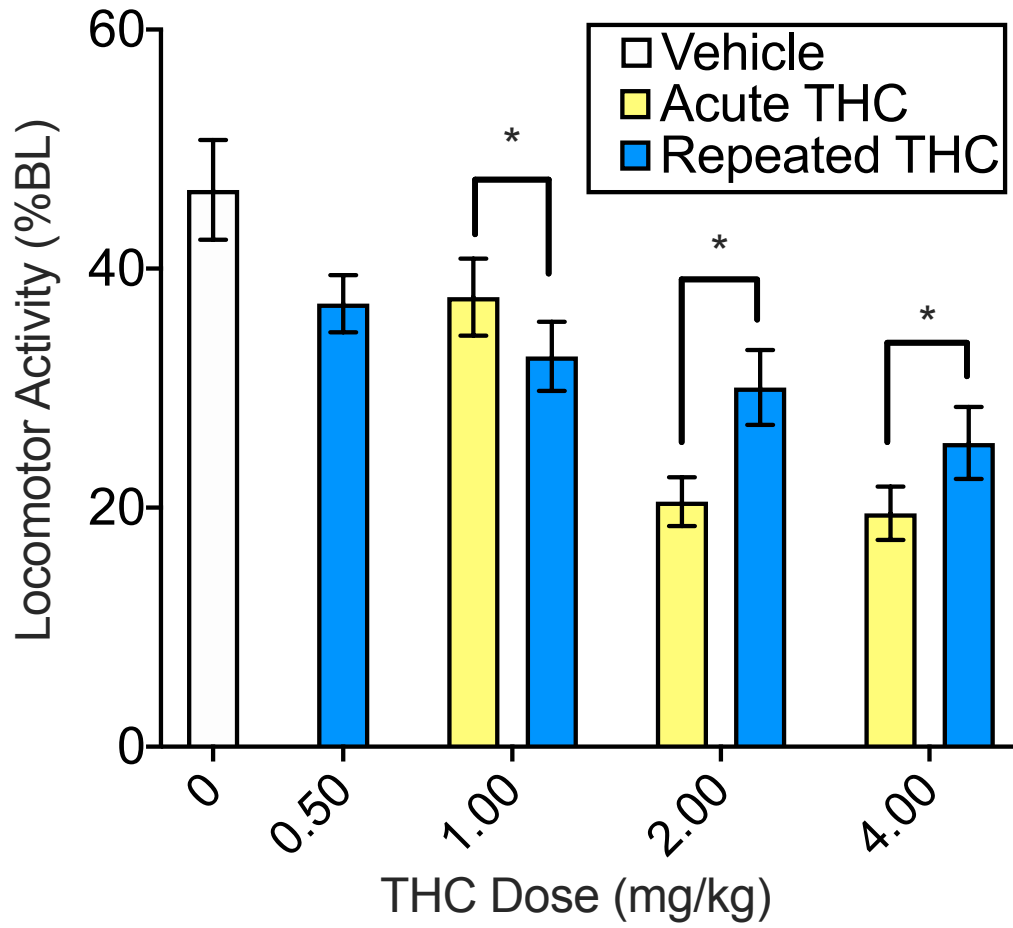
Supplemental Figure 4



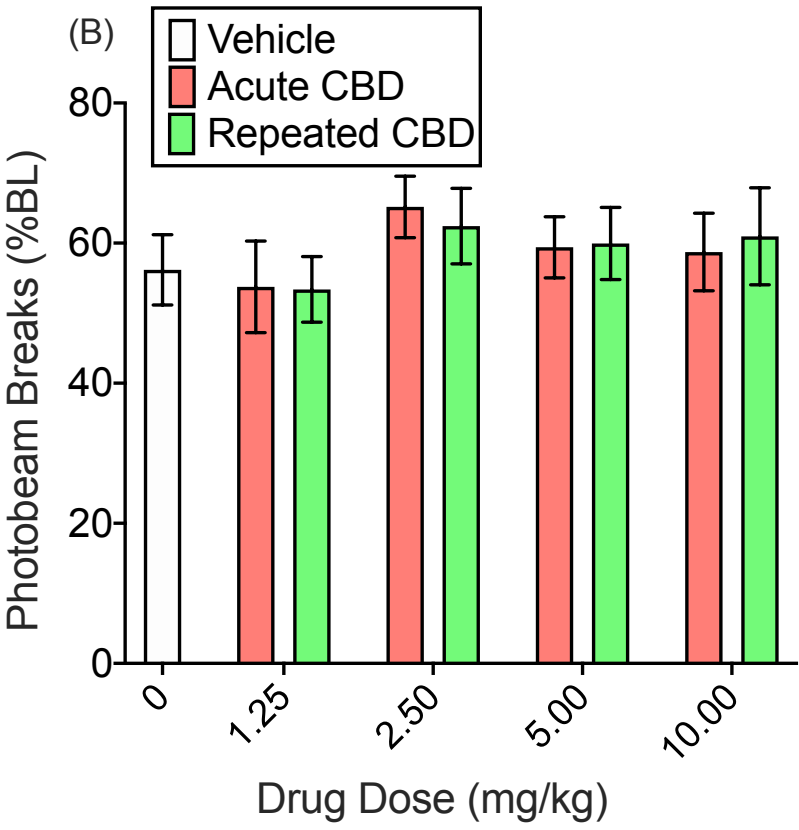
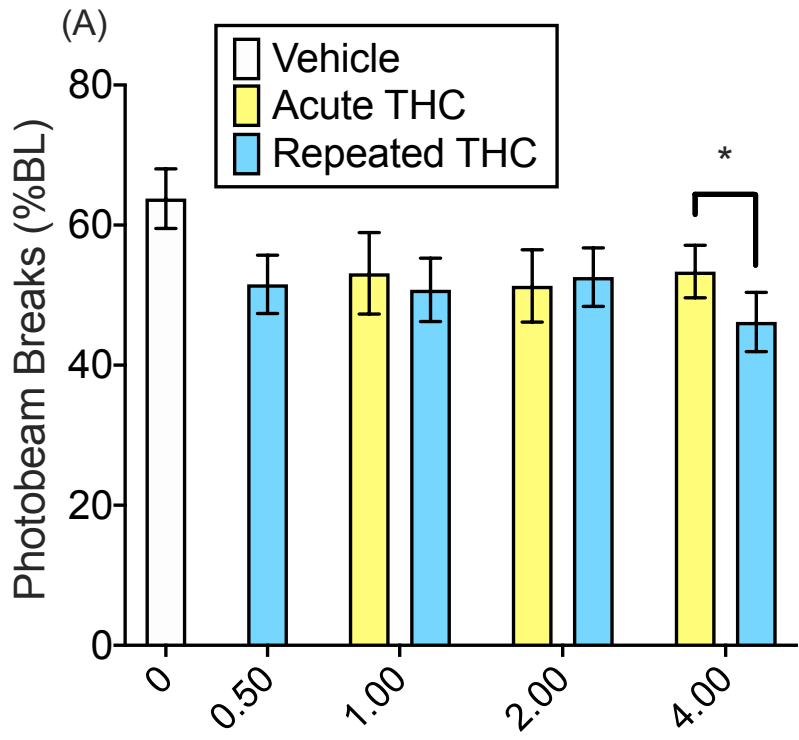
Supplemental Figure 5



Supplemental Figure 6



Supplemental Figure 7



Supplemental Figure 8

